CASE REPORTS

Subarachnoid Hemorrhage Subsequent to Injection of Epinephrine

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AN instance is reported of subarachnoid hemorrhage in a middle-aged male during an acute asthmatic attack while under treatment with repeated subcutaneous injections of epinephrine.

CASE REPORT

The patient, aged 56, entered Samuel Merritt Hospital on October 28, 1946, complaining of slight difficulty in breathing, headache and low back pain. For 15 years he had suffered from perennial recurrent attacks of bronchial asthma, characterized by severe wheezing, shortness of breath, paroxysmal coughing and expectoration of tenacious mucoid sputum. He first came under the treatment of one of us (A.H.R.) in September, 1946, at which time a cereal-free elimination diet (Rowe) 1, 2 and 3 was prescribed and the patient was advised to use tedral tablets and a 1:100 epinephrine nebulizer for symptomatic relief. Initially there was improvement, but ten days prior to admission he was placed in another hospital because of a severe asthmatic attack which followed the unintentional ingestion of milk and wheat. Treatment consisted of the establishment of a dust-free environment, continuation of the diet and subcutaneous injections of 1:1,000 epinephrine in doses of from 0.5 cc. to 0.7 cc. every four to five hours.

Nine days prior to entry, while in the former hospital, a subcutaneous injection of 0.7 cc. of 1:1,000 epinephrine was given. Immediately after the injection the patient complained of severe tremor, rapid heart action and weakness and told a nurse that epinephrine had never previously had such effect. Within five or six hours after this injection the patient noted the gradual onset of lumbar backache, occipital headaches and malaise. These symptoms were persistent and were partially relieved by codeine and aspirin and changes of position. The severe asthma subsided and he was discharged on the fifth day with only slight difficulty in breathing, but still complaining of backache, headache and malaise. During the next five days there was further decrease in asthma, but headache and backache increased. On the day of admission to the hospital severe asthma developed and the headache and backache increased markedly.

System Review: A diffuse papular eruption had developed following the administration of a saturated solution of potassium iodide three weeks prior to entry. There had been rare frontal headaches of brief duration throughout the patient's life and for ten to fifteen years he had noted frequent pains in the elbows, knees and lower back. Sour stomach and gaseous eructations following the ingestion of fruits had been experienced for many years. For one month prior to entry he had complained of nocturia, burning and frequency of urination.

The medical and family history were non-contributory.

Physical Examination: On entry, blood pressure was 150 mm. of mercury systolic and 90 diastolic, pulse was 68, respirations 16 per minute, and temperature 98.6° F. The patient was a well developed, well nourished, middle-aged white male who lay quietly in bed and seemed moderately depressed. Positive findings included slight limitation of neck flexion to approximately 30 degrees, beyond which point pain and rigidity in the posterior nuchal muscles were produced. Retinal arteries showed sclerotic changes, grade II. Both lung fields were hyperresonant and wheezes on prolonged expiration were generally audible. A right indirect inguinal hernia was present. The prostate was enlarged and tender with a palpable firm nodule in the upper aspect of the left lobe. Straight leg raising bilaterally caused low back pain. Abdominal, cremasteric, patellar and achilles reflexes were absent. The examination was otherwise negative.

Hospital Course: The day following entry increased neck stiffness was noted and nausea and vomiting developed. Because of persistent vomiting glucose and saline solutions were given intravenously as necessary. On the third hospital day the patient complained of double vision. Neurological examination did not elicit additional findings. A urologist found chronic prostatitis and prostatic hypertrophy, grade III. By the fourth day stiffness of the neck and double vision were more pronounced. Lumbar puncture revealed grossly bloody fluid which was xanthochromic after centrifugation. Initial pressure was 280 mm. of water. Result of the Queckenstedt test was normal. Following lumbar puncture there was immediate partial relief of the stiff neck and back pain with increased range of neck flexion. Two days later fever (maximum 101° F.), present since entry, disappeared. On the fifth day the neurologist confirmed the diagnosis of subarachnoid hemorrhage. He found definite impairment of the function of the right external rectus muscle with poor conversion. During the following six days there was a gradual disappearance of symptoms with a return of the patient's normal mental status. Lumbar puncture on the eleventh hospital day revealed no blood, but xanthochromia persisted. The pressure was 160 mm. of water. During hospitalization the asthma rapidly disappeared. The patient was discharged symptom-free on the 16th day.

Subsequently he was seen at monthly intervals for eight months, and there was no return of symptoms referable to the central nervous system. In January, 1947, the inguinal hernia was uneventfully repaired under spinal anesthesia.

Laboratory and X-ray: A roentgenogram of the chest taken prior to entry revealed minimal parenchymal changes

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suggestive of silicosis. Examination of the urine showed specific gravity of 1.022, no albumin or sugar, and a diacetic acid content of 3 plus. Examination of the blood showed a hemoglobin value of 93 per cent. Erythrocytes numbered 4.67 million and leukocytes 9,600. Results of a Kline test were negative. The erythrocyte sedimentation rate (Linzenmeier method) on the seventh hospital day was 18 mm. in more than two hours. On the eighth day the acid phosphatase was 0.2 unit. Roentgenograms of the skull taken on the tenth day showed no evidence of pathologic changes. Roentgenograms of the lumbar and sacroiliac spine showed marked narrowing of intervertebral discs between the body of the fifth lumbar vertebra and the sacrum, and there were moderate osteoarthritic changes involving the lower thoracic and upper lumbar vertebral bodies.

DISCUSSION

Flexner and Schneider[1] in 1938 first reported subarachnoid hemorrhage following the subcutaneous injection of a single dose of 1:1,000 epinephrine in a 20-year-old woman suffering from urticaria, 14 days postpartum. Delivery had been performed with low forceps, but was uneventful. They postulated that if a congenital aneurysm were present, it may have been weakened by the strain of labor and that a possible sudden rise in blood pressure with increased cerebral circulation volume and velocity following the injection of epinephrine was sufficient to cause rupture of the aneurysm. The possibility that some epinephrine entered the venous circulation was also considered. These authors also reviewed the literature dealing with the effects of epinephrine on the cerebral circulation.

We believe that in our patient the subarachnoid hemorrhage probably resulted from the entrance of some of the subcutaneously injected epinephrine into the venous circulation. This was indicated by the severe tremor, tachycardia and weakness which immediately followed the injection of epinephrine on the ninth day prior to admission. The subsequent train of symptoms, physical findings and laboratory findings was typical of subarachnoid hemorrhage. The neurological findings indicated that the hemorrhage probably occurred from a vessel at the base of the brain. The presence of a congenital aneurysm or area of decreased resistance secondary to arteriosclerotic changes in the basilar vessels must be considered. With such an area of decreased resistance the sudden rise in blood pressure with increased cerebral circulation volume and velocity might have been sufficient to cause rupture and hemorrhage into the subarachnoid space.

SUMMARY

An instance of subarachnoid hemorrhage in a middle-aged male during an acute attack of bronchial asthma treated by repeated subcutaneous injections of 0.5 cc. to 0.7 cc. of 1:1,000 epinephrine is reported. We believe that hemorrhage probably resulted from entrance of some of the subcutaneously injected epinephrine into the venous circulation.

REFERENCES

1. Flexner, M., and Schneider, B.: Subarachnoid hemorrhage subsequent to injection of epinephrine, Ann. Int. Med., 12:876-882 (Dec.), 1938.

Acanthosis Nigricans with Unusual Cutaneous and Clinical Features

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ALMOST from its earliest recognition acanthosis nigricans has been associated with the problem of malignancy. In this country we automatically assume the juvenile type to be benign and the adult type to be associated with a malignant neoplasm. Some of the European observers apparently do not hold this view, but feel that a large percentage, even of the adult type, is of a benign character.

The customary course of acanthosis nigricans is to develop increased markings of the skin up to the formation of verrucae and even peduncula in the various folds of the body such as the neck, axillae, and groins, usually associated with papule formation to a moderate degree in other areas. Mostly the skin manifestations are in evidence a considerable time before the patient complains of systemic symptoms. This time interval may be a considerable number of years and usually the course of events is chronic, which probably accounts for the discrepancy among views as to the etiologic nature of the disease.

We shall not review the various theories evolved to explain the course of events in acanthosis nigricans since we have no definite knowledge of it. Manifestly there must be a mechanism involved that does not come to play in the ordinary case afflicted with carcinoma. In the case reported here the course of events was almost the reverse of that usually seen.

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CASE REPORT

A woman, 49 years of age, was seen by us for the first time on June 22, 1945. She then presented innumerable verrucous, discrete papules over almost the entire body. There was, however, little or no acanthosis in the usual areas. While a suspicion of acanthosis nigricans could be entertained, a positive diagnosis was impossible. The papules, according to the patient, had been present for about six weeks. Family and past personal history was irrelevant. About two months before we saw her she had consulted her family physician for the first time because of obesity. Evidently, after taking a complete history and making a thorough physical examination, he found nothing of much importance and placed her on a reduction diet. During the week that elapsed before her next visit to the physician a non-productive cough had developed but it had subsided before another visit seven weeks later. At that time the physician noted a considerable growth of "verrucous masses" on various areas of the glabrous skin, and two weeks later these masses covered practically the entire skin. The patient was then referred to us late in June. We did not have opportunity to observe the patient further until late July. Meanwhile a surgeon who examined her suspected ovarian cysts. Evidently disease of the stomach was not suspected despite a complaint of much belching of gas and bad taste in the mouth. X-ray examination at that time showed a fleck of barium retention in the duodenum after six hours, which was interpreted as indicating duodenal ulcer. The surgeon, evidently impressed by the large abdominal tumor masses, removed two large ovarian tumors in July. These were pronounced metastatic carcinomas by the pathologist. We observed the patient again at the hospital on July 27, when the eruption also showed in the